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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/373,984	08/16/99	SU X	70862/93137

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HM12/1005

EXAMINER	
TUNG, J	
ART UNIT	**PAPER NUMBER**
1656	6

DATE MAILED: 10/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/373,984	Su et al.
Examiner	**Group Art Unit**
Joyce Tung	1656

☒ Responsive to communication(s) filed on *Jul 13, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-24* is/are pending in the application.

Of the above, claim(s) *14-19* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-13 and 20-24* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ notice to comply

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, claims 1-13 and 20-24 in Paper No. 4 is acknowledged.

2. Claims 14-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups II-IV, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 4, since there is no an argument made in the response to the restriction requirement. Thus, the election was made without traverse.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper tames extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.d. 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 5-8 and 10-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17, 24-43 and 50-69 of copending Application No. 09/285,658. Although the conflicting claims are not identical, they

are not patentably distinct from each other because instant claims 5-8 and 10-22 are drawn the method which is included in the claims 1-17, 24-43 and 50-69 of copending Application No. 09/285,658 in which claims 1-17, 24-43 and 50-69 are drawn to a method of proportional amplification of nucleic acid comprising creating fragments of a single-stranded DNA population, synthesizing double-stranded DNA from the fragment of the single stranded DNA population and producing multiple copies of sense RNA from the double-stranded DNA, the amplified DNA is detected. Thus, this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-13 and 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-13 are 20-24 are vague and indefinite because of the language "in a single phase". It is unclear what it is meant by the language, for example, does it mean that the amplification is occurred in a single steps or in a solution phase or on a solid support. It is suggested to clarify uncertainty.

b. Claim 2 is vague and indefinite because of the language "proportional". Based upon the claim language of claim 1, there are two steps in which the one is to synthesize double-stranded DNA and the second step is to produce multiple copies of RNA. It is unclear which amplification is proportional. Further, it is unclear what it is meant by the language "proportional". Does it meant that the amplification is linear or exponential. It is suggested to clarify uncertainty.

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwoh et al. (Proc. Natl. Acad. Sci. USA, 1989, Vol. 86, pg. 1173-1177).

Kwoh et al. disclose a method of amplifying RNA involving a double stranded cDNA synthesis and then the cDNA is used as template to produce multiple copies of RNA (See pg. 1171, the Abstract). The target nucleic acid can be total RNA (See pg. 1173, column 2, fifth paragraph) or DNA (See pg. 1173, the Abstract). The total RNA inherits that there is mRNA included. The amplified products are detected with the use of a slot-blot apparatus comprising nucleic acid probes (See pg. 1174, column 1, second paragraph). The amplified products are also detected by sephacryl beads containing nucleic acid probes (See pg. 1174, column 1, third

paragraph). Since the total RNA is from HIV-1-infected lymphocyte cells, this indicates that the infected cells must be eukaryotic cell. The cells must also be human cells which are mammalian cell. Based upon the description of the procedure of amplifying RNA, there is no indication that an extraction or precipitation occurred during the procedure) (See pg. 1174, second paragraph). This is the same as the indication in the specification that the reaction can occur in one phase which is without organic extracting and precipitation (See pg 5, lines 25-28).

The teachings of Kwoh et al. anticipate the limitations of Instant claims 1-12. Instant claims 1-12 are drawn to a method of amplifying nucleic acid which is proportional amplification. The method involves synthesizing double-stranded DNA from a single-stranded DNA population and producing multiple copies of RNA from the double-stranded DNA in a single phase. The target nucleic acid is genomic DNA, and RNA from eukaryotic cell which is mammalian, dissected tissues or brain cell. The varieties of cells are listed in claim 12. The amplified products are detected by attaching to a solid support comprising a nucleic acid probe.

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwoh et al. (Proc. Natl. Acad. Sci. USA, 1989, Vol. 86, pg. 1173-1177) in view of Goller et al. (Oncogene, 1998, Vol. 16, pg. 2945-2948).

The limitations of instant claim 1 are rejected under 35 U.S.C. 102(b) anticipated by the teachings of Kwoh et al. set forth in section 6 above.

Goller et al. disclose the analysis of differential gene expression in v-jun-transformed chicken embryo fibroblasts (CEF) compared to normal CEF by using tag PCR subtraction method (See the Abstract). The target is from mRNA of CEF (See pg. 2946, fig. 2).

The teachings of Kwoh et al. and Goller et al. suggest the limitations of claims 1 and 13. Instant claim 13 recites further limitations of claim 1 in which the target RNA is from embryonic and tumorigenic cell or tissues.

One of ordinary skill in the art at the time of the instant invention would have been motivated to use RNA from embryonic and tumorigenic as target as taught by Goller et al. in the method of Kwoh et al. because the expression of the glutaredoxin mRNA could be induced by a jun-estrogen receptor chimaera in the absence of *de novo* protein biosynthesis and therefore the

oncogene can be studied (See the Abstract). It would have been prima facie obvious to carry out the method as claimed.

9. Claims 1 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwoh et al. (Proc. Natl. Acad. Sci. USA, 1989, Vol. 86, pg. 1173-1177) in view of Compton (Nature, 1991, Vol. 350(7), pg. 91-92).

The limitations of instant claim 1 are rejected under 35 U.S.C. 102(b) anticipated by the teachings of Kwoh et al. set forth in section 6 above.

Kwoh et al. do not disclose a kit which is used to fulfil the amplification process.

Compton discloses a method of amplifying RNA involving using the kit containing the components and appropriate primers.

The teachings of Kwoh et al. and Compton suggest the limitations of instant claims 1 and 22-24. Instant claims 22-24 recite further limitations to claim 1 in which the kit is used for the method.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine these references of Kwoh et al. and Compton to make instant invention for a reasonable expectation of success because the method of Kwoh et al. allows the detection of fewer than one HIV-1 infected lymphocyte cell in a population of 10^6 uninfected lymphocyte cells and the kit of Compton is convenient to perform the method which is well known in the art at the time of the instant invention. It would have been prima facie obvious to make the kit as claimed.

10. Claims 1 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwoh et al. (Proc. Natl. Acad. Sci. USA, 1989, Vol. 86, pg. 1173-1177) in view of Schnipelsky et al. (5,229,297).

The limitations of instant claim 1 are rejected under 35 U.S.C. 102(b) anticipated by the teachings of Kwoh et al. set forth in section 6 above.

Kwoh et al. do not disclose the method which is involved using an automated machine.

Schnipelsky et al. disclose an apparatus to amplify a nucleic acid sequence (See column 2, lines 17-24). The apparatus involves PCR thermocycler (See column 14, lines 7-9), an integrated reaction device and a robotic delivery system (See column 9, lines 26-60).

The teachings of Kwoh et al. and Schnipelsky et al. suggest the limitations of instant claims 1 and 20-21. Instant claims 20-21 recite further limitations to instant claim 1 in which the method is performed by an automated machine including a PCR thermocycler, an integrated reaction device and a robotic delivery system.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the references of Kwoh et a. and Schnipelsky et al. because the method of Kwoh et al. allows the detection of fewer than one HIV-1 infected lymphocyte cells in a population of 10^6 uninfected lymphocyte cells and the apparatus of Schnipelsky et al. can prevent sample contamination (See column 2, lines 17-24). It would have prima facie obvious to carry out the method as claimed.

Sequence Rules

13. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Additionally, all nucleic acid sequences in the specification are required to have SEQ ID NO, for example, the primer (See pg. 5 and 13).

Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

14. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached at (703) 308-1152.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

15 Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1656 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

September 27, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

10/1/00